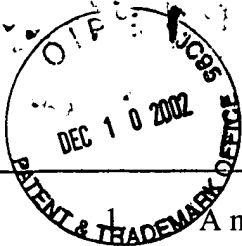


CLEAN CLAIM SHEETS



β^1 A method of preventing the formation of inhibitory antibodies to a blood coagulation protein delivered to a mammal by way of gene therapy, said method comprising administering to said mammal cyclophosphamide or anti-CD40 ligand prior to or simultaneously with said gene therapy or before formation of said inhibitory antibodies, the delivered blood coagulation protein being the same species as said mammal.

$N.E.$ 2. The method of claim 1, wherein said mammal and gene are human.

β^2 3. The method of claim 1, wherein said gene therapy is delivery of a nucleic acid encoding Factor IX to said mammal, which when expressed in said mammal, an increase in Factor IX is observed in said mammal.

β^3 4. The method of claim 1, wherein said delivered blood coagulation protein is selected from the group consisting of Factor VII, Factor VIII, Factor IX, and Factor X.

5. The method of claim 1, wherein said gene therapy is delivery of Factor IX to said mammal.

6. The method of claim 1, wherein said gene therapy is performed by administering a viral vector to said mammal, wherein said viral vector comprises a nucleic acid to be delivered to said mammal.

7. The method of claim 6, wherein said viral vector is an adeno-associated viral vector.

8. The method of claim 5, wherein said Factor IX is delivered to said mammal using an adeno-associated virus vector.

9. The method of claim 1, wherein said immunosuppressive agent is cyclophosphamide.

β^4 10. The method of claim 1, wherein said mammal has hemophilia B and said inhibitory antibodies specifically bind with Factor IX protein.

11. A method of reducing formation of an inhibitory antibody to a blood coagulation protein delivered to a mammal by way of gene therapy, said method comprising administering to

said mammal an immunosuppressive agent prior to or simultaneously with said gene therapy or before formation of said inhibitory antibodies, the delivered blood coagulation protein being the same species as said mammal.

12. A method of reducing formation of an inhibitory antibody to a protein delivered to a human by way of gene therapy, said method comprising administering to said human an immunosuppressive agent prior to or simultaneously with said gene therapy or before formation of said inhibitory antibodies, the delivered protein being human.
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13. The method of claim 13, wherein said gene therapy is delivery of a nucleic acid encoding Factor IX to said mammal, which when expressed in said mammal, an increase in Factor IX is observed in said mammal.

14. The method of claim 13, wherein said delivered blood coagulation protein is selected from the group consisting of Factor VII, Factor VIII, Factor IX, and Factor X.

15. The method of claim 13, wherein said gene therapy is delivery of Factor IX to said mammal.

16. The method of claim 13, wherein said gene therapy is performed by administering a viral vector to said mammal, wherein said viral vector comprises a nucleic acid to be delivered to said human.
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17. The method of claim 18, wherein said viral vector is an adeno-associated viral vector.

18. The method of claim 17, wherein said Factor IX is delivered to said mammal using an adeno-associated virus vector.

19. The method of claim 13, wherein said immunosuppressive agent is selected from the group consisting of cyclophosphamide, FK506, anti-CD40 ligand, CTLA4Ig, cyclosporin, antiB71-B72, and an immunosuppressive steroid.

20. The method of claim 13, wherein said immunosuppressive agent is cyclophosphamide.

21. The method of claim 13, wherein said mammal has hemophilia B and said inhibitory antibody specifically binds with Factor IX protein.

B⁶ 22. The method of claim 1, wherein said mammal has no detectable endogenous expression of the delivered blood coagulation protein.

23. The method of claim 13, wherein said mammal has no detectable endogenous expression of the delivered blood coagulation protein.

B⁷ 24. The method of claim 1, wherein said immunosuppressive agent is administered concomitantly with said gene therapy.

B⁸ 25. The method of claim 13, wherein said immunosuppressive agent is administered concomitantly with said gene therapy.

26. 30. The method of claim 14, wherein said gene therapy is delivery of a nucleic acid encoding Factor IX to said mammal, which when expressed in said mammal, an increase in Factor IX is observed in said mammal.

27. 31. The method of claim 14, wherein said delivered protein comprises a blood coagulation protein.

28. 32. The method of claim 31, wherein said blood coagulation protein is selected from the group consisting of Factor VII, Factor VIII, Factor IX, and Factor X.

29. 33. The method of claim 14, wherein said gene therapy is delivery of Factor IX to said mammal.

30. 34. The method of claim 33, wherein said Factor IX is delivered to said mammal using an adeno-associated virus vector.

31. 35. The method of claim 14, wherein said gene therapy is performed by administering a viral vector to said mammal, wherein said viral vector comprises a nucleic acid to be delivered to said mammal.

32. The method of claim 35, wherein said viral vector is an adeno-associated viral vector.

33. The method of claim 14, wherein said immunosuppressive agent is selected from the group consisting of cyclophosphamide, FK506, anti-CD40 ligand, and CTLA4Ig.
34. The method of claim 14, wherein said immunosuppressive agent is cyclophosphamide.
35. The method of claim 14, wherein said human has hemophilia B and said inhibitory antibodies specifically bind with Factor IX protein.